## REMARKS

Claims 1-14 and 65, 66, and 71 constitute the pending claims in the present application. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

1.     Claims 65 and 66 have been withdrawn from consideration as directed to a nonelected invention or species. Applicants note that claims 65 and 66 were previously rejoined with the elected invention of Group I. Applicants acknowledge, however, that claims 65 and 66 are directed to a nonelected species and will be considered only upon indication of allowable subject matter.

2.     Applicants note with appreciation that the Information Disclosure Statement filed March 30, 2005 has been considered in full.

3.     Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants traverse this rejection.

The Examiner alleges that the list recited in claim 7 includes both genes and proteins, and that it is unclear whether Applicants intended the claimed informative genes to include genes, proteins, or both. The Examiner's concern appears to be based solely on the fact that certain genes in the list are capitalized.

Although Applicants agree that certain of the recited gene names are capitalized, this alone is an insufficient basis to reject the claim. Specifically, although capitalization is a useful convention for distinguishing gene names from protein names, it is by no means an immutable law. One of skill in the art would not rely on capitalization alone to interpret the claimed invention. In light of the specification considered as a whole, one of skill in the art would readily appreciate the metes and bounds of the claimed subject matter.

To briefly illustrate how the specification clarifies any alleged confusion, Applicants direct the Examiner's attention to Figure 3B and the discussion of Figure 3B provided at page 46, line 21-page 47, line 28. Figure 3B depicts Applicants' analysis of the informative genes explicitly recited in claim 7. Note that in Figure 3B, all of the gene names are capitalized.

However, the text clearly indicates that the experiments summarized in Figure 3B analyzed gene expression of informative genes.

Applicants note that the specification clearly appreciates that the claimed methods can be used to classify samples based not only on expression of informative genes but also on expression of proteins encoded by informative genes (See, for example, page 21, lines 1-13). However, based on the particular experiments used to measure expression of informative genes or proteins encoded therefrom (e.g., nucleic acid-based microarrays versus protein detection methodologies), one of skill in the art can readily ascertain the metes and bounds of the claimed subject matter.

Applicants contend that the specification provides ample context such that one of skill in the art can readily appreciate the metes and bounds of the claimed subject matter. Reconsideration and withdrawal of this rejection are respectfully requested.

4.      Claims 1-14 and 71 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Zheng *et al.* (IEEE Transactions on Neural Networks, 1997, 8: 1386-1396) in view of Eisen *et al.* (IDS ref AV: Proceedings of the National Academy of Science, 1998, 95: 14863-14868) and Barnhill *et al.* (US Patent No. 6,760,715) Applicants respectfully traverse this rejection.

Applicants contend that the cited references fail to undermine the patentability of the claimed invention. Applicants disagree with the entire basis of the rejection, whereby the teachings of three references were cobbled together and viewed with impermissible hindsight in light of the teachings of the present application. Furthermore, Applicants do not agree with the description or characterization of the teachings of Zheng *et al.*

However, despite Applicants' disagreement with the basis of the rejection and the characterization of the teachings of Zheng *et al.*, Applicants' traversal is based on a more fundamental flaw in the rejection. Specifically, Applicants contend that teachings of Barnhill *et al.* relied upon by the Examiner are not available as prior art against the present application for the reasons provided below. Given that the remaining references, standing alone, do not teach or suggest each and every limitation of the claimed invention, the remaining references fail to

satisfy the criteria necessary to render the claimed invention obvious. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

The effective filing date of the present application is April 9, 1999. The Barnhill *et al.* patent cited by the Examiner (US Patent No. 6,760,715) claims priority to a number of United States utility and provisional applications. Only one of those applications, US provisional application serial number 60/083,961 (the "'961 application"), filed May 1, 1998, was filed prior to the effective filing date of the present application. Accordingly, to support the rejection, the '961 application must teach that which the Examiner relies upon to undermine the patentability of the presently claimed invention. Simply put, this priority document fails to do so.

In the previous Office Action, the Examiner alleged that "Barnhill teaches analysis of gene expression patterns involved in various cancers using a linear discriminant classifier; i.e. weighted voting and clustering. Barnhill teaches use of his SVM system to classify leukemia data, specifically to differentiate ALL from AML." (Office Action, page 5). The Examiner has relied upon these aspects of Barnhill, in combination with the teachings of Zheng *et al.* and Eisen *et al.*, to allegedly render the claimed invention obvious.

Applicants enclose herewith a copy of US provisional application serial number 60/083,961, filed May 1, 1998 (enclosed herewith as Exhibit 1). The '961 application totaled six pages and prophetically disclosed general methods of organizing large amounts of data. The general and prophetic nature of this provisional application is aptly reflected in its title: A Method for Discovering Knowledge Using Support Vector Machines. The '961 application did not teach the use of the SVM system to classify leukemia data, particularly to differentiate ALL from AML. In fact, the '961 application provided little more than the state of the art of SVM technology.

The '961 application was the only Barnhill priority document filed before Applicants' effective filing date, and the '961 application fails to teach the subject matter relied upon by the Examiner to support the present rejection. Accordingly, Barnhill fails to support the rejection under 35 U.S.C. 103(a). Whether subject matter disclosed in subsequently filed Barnhill priority documents undermines the patentability of the present invention is irrelevant because such teachings are not prior art against the present application.

Applicants' contention that the '961 application fails to undermine the patentability of the presently claimed invention is further supported by a review of a subsequently filed Barnhill priority document. US provisional application serial number 60/161,806 (the "'806 application"; enclosed herewith as Exhibit 2) was filed after the effective filing date of the present application on October 27, 1999. Although the '806 application is not available as prior art, the disclosure sheds particular light on the relationship between the teachings of Barnhill and Applicants' invention. In the '806 application, the inventors used SVM analysis to perform preliminary experiments on the leukemia data of Golub *et al.* Specifically, the inventors analyzed data published by Golub *et al.* in a paper entitled "Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring." (page 1 of the '806 application). The analyzed dataset included samples of ALL and AML. It is this aspect of Barnhill *et al.* that the Examiner appears to rely upon to support the present rejection under 35 U.S.C. 103(a).

Applicants note that the dataset analyzed in the '806 application was generated by the inventors of the present application. More particularly, the dataset analyzed in the '806 application is the ALL and AML data included in the present application and used by Applicants to support the presently claimed invention. Preliminary and subsequent analysis of this ALL and AML data first appeared in the provisional applications to which the present application claims priority. For example, analysis of this ALL and AML data appeared in provisional application serial number 60/128,664, filed April 9, 1999, as well as provisional application serial number 60/135,397, filed May 21, 1999. Thus, the teachings of Barnhill that allegedly undermine the patentability of the presently claimed invention were actually based on Applicants' invention and have an effective date later than Applicants' priority date.

The teachings of Barnhill relied upon by the Examiner to support the rejection under 35 U.S.C. 103(a) are not available as prior art against the present application. The remaining references, standing alone, do not teach or suggest the claimed invention, and thus fail to support the rejection under 35 U.S.C. 103(a). Applicants note for the record that Applicants do not necessarily agree with the Examiner's characterization of the remaining references (Zheng *et al.* and Eisen *et al.*). Applicants reserve the right to argue against the Examiner's characterization of

these references, if necessary, in subsequent responses.  Reconsideration and withdrawal of this

rejected are respectfully requested.

## CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000.
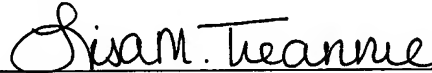
Please charge any deficiency or credit any overpayment in the fees that may be due in this matter to **Deposit Account No. 18-1945**, from which the undersigned is authorized to draw, under **Order No. WIBL-P02-518**.

Respectfully Submitted,

Date: <u>August 12, 2005</u>

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